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10/018,697	06/18/2002	Thomas D Reed	91830/0503228	7783

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1633	

NOTIFICATION DATE	DELIVERY MODE
08/27/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/018,697	REED ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10 and 12-51* is/are pending in the application.

4a) Of the above claim(s) *38-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-10 and 12-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt and entry of the amendment dated 6/5/2007 is acknowledged. After entry of the amendment, claims 1, 3-10 and 12-51 are pending. Claims 38-51 remain withdrawn as directed to a non-elected invention. Claims 1, 3-10 and 12-37 are under examination.

Claim Objections

Claim 1 objected to because of the following informalities: "extrachromasomal" in line 1 should be "extrachromosomal". Appropriate correction is required.

Claim 21 objected to because of the following informalities: "comprising" in line 2 should be "comprises". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-10 and 12-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by amendment of the claims. This is New Matter rejection.**

Amended claim 1 (from which all other claims depend) recites in step d): "wherein step (d) is performed prior to, after, or concurrently with step (c)." Step d) is a step of contacting the biological sample with a chaotropic solution, and step c) is contacting the sample with a ribonuclease (e.g. RNAse). The response does not indicate where support for the amendment may be found in the specification as originally filed. The original claims (claim 2) and specification (page 10, lines 13-17; page 11, line 18 to page 12, line 14; and the Examples) only disclose contacting the biological sample with an RNAse before contacting the sample with the chaotropic solution. Therefore, there appears to be no support for the limitations wherein step (d) of claim 1 is performed prior to, or concurrently with step (c). Thus, the amended claims include impermissible New Matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29 and 31 contain the trademark/trade names TRITON, Tween 20, Tween 30, Tween 80 and TRITON X-114, respectively. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade

name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a detergent and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-10, 12-30, and 32-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little (U.S. 5,075,430, 1991, of record) as evidenced by Sigma-Aldrich catalog entry for Trizma hydrochloride (2007), in view of Padhye et al (5,658,548, 1997, of record), Koller (U.S. 5,128,247, 1992) and Chomczynski (U.S. 5,945,515, 1999, effective filing date 7/31/1995). **This rejection is maintained for reasons (in part) made of record in the Office Action dated 1/11/2005, and for reasons set forth below. Upon further consideration, additional claims and prior art are applicable to this rejection, hence, it is considered a new ground of rejection.**

Little discloses a DNA purification method comprising alkaline lysis of bacteria followed by neutralization and removal of proteins and chromosomal DNA by centrifugation. The supernatant (containing plasmid DNA) was precipitated, dried, and resuspended in TE (0.05 M Tris-Cl pH 8, and 10.0 mM ethylenediaminetetraacetic acid (EDTA)) and 6 M $NaClO_4$ (sodium perchlorate, a chaotropic agent), see column 3, lines 63-68 and Examples 1 and 2, beginning in column 7. A Celite (diatomaceous earth) slurry was added and then the sample centrifuged (precipitation of plasmid DNA, bound to the diatomaceous earth). The Celite pellet was washed twice with a buffer of 50% ethanol, which is considered to be "adding an amount of organic solvent effective to precipitate" the plasmid DNA, e.g. step e) of claim 1. This is because step e) only requires adding an effective amount of the solvent "effective to precipitate" the plasmid DNA and thus does not require any actual precipitation, only that an effective amount of the organic solvent be added. Little et al teach that the ethanol-containing buffer is effective to

precipitate the DNA (i.e. keep the DNA out of solution) at a range of from 20-95% ethanol (column 4, lines 6-20). DNA was eluted from the Celite precipitate with TE and used in restriction and ligation reactions (column 7, lines 24-60 and Table A). Regarding claim 16, the 6M $NaClO_4$ taught above is considered to be "about" 5M. This is because the instant specification does not define the interpretation of "about", hence, the term is interpreted broadly to encompass chaotropic agents at concentrations close to 5M that achieve the claimed function, i.e. effective to create a chaotropic environment. Regarding claim 17, the TE buffer (pH 8, column 4, lines 55-57) used to resuspend the DNA pellets(s) comprises Tris-Cl (see above), which is a synonym for tris(hydroxymethyl)aminomethane and hydrogen chloride (see Trizma hydrochloride entry from the Sigma catalog). Regarding claim 28, the MW of EDTA is 292.25, thus a 10mM solution (as above) contains 0.29g/ 100 ml of EDTA, which is a 0.29% solution of EDTA.

Little does not explicitly teach the use of a ribonuclease enzyme, or a chaotropic solution comprising: a reducing agent; a detergent; a salt as in claim 24; a solvent as in claim 32; or an antioxidant as in claim 37.

Padhye et al teach a plasmid purification protocol comprising alkaline lysis of *E. Coli* in a buffer containing RNase A followed by neutralization and centrifugation to remove proteins and chromosomal DNA (column 11, line 36 - column 12, line 7). To the supernatant (containing plasmid DNA) was added a resin comprising guanidine chloride (a chaotropic agent) and glass particles that bind DNA under these conditions. The guanidine chloride solution may comprise EDTA at from 5 to 15 mM (column 6, lines 19-38), which meets the limitations of claim 27 for reasons set forth above. The glass particles were precipitated by filtration and centrifugation,

washed, and DNA eluted with TE buffer (column 13, lines 21-65). The TE buffer is pH 7.5 (column 11, Example 3), comprises Tris-Hcl, and thus meets the limitations of claims 17-20 for reasons et forth above. Furthermore, the glass particles were washed with a solution comprising ~ 50% ethanol (Column Wash Solution, column 11, Example 3) which is considered to be "adding an amount of organic solvent effective to precipitate" the plasmid DNA, e.g. step e) of claim 1. This is because step e) only requires adding an effective amount of the solvent "effective to precipitate" the plasmid DNA and thus does not require any actual precipitation, only that an effective amount of the organic solvent be added. Effective concentration ranges of the chaotropic ions are at least 2M and above, or above 5M before addition of DNA, and is preferably of 5-7M (column 5, line 65 to column 6, line 19), or may be 4M (Example 9, column 18 or Table 3, column 20).

Padhye et al do not teach precipitating plasmid DNA prior to step (c) of claim 1 (i.e. claim 3), or a chaotropic solution comprising: a reducing agent; a detergent; a salt as in claim 24; a solvent as in claim 32; or an antioxidant as in claim 37.

Koller teaches a method of DNA purification comprising dissolving cells in a nucleic acid releasing composition (4M guanidium isothiocyanate, 25mM Na Citrate pH 7.0, 0.5% sarcosyl, 0.1M mercaptoethanol and 0.5M Na acetate, column 9, lines 23-33 and column 10, lines 16-22) followed by addition of 2.5 volumes of ethanol and precipitation (column 9, lines 34-45 and claim 1). Isopropanol may be used in place of ethanol at about a 50% concentration (e.g. claims 33-34), see column 7, lines 21-31. Sarcosyl is a detergent, and may be replaced with any anionic detergent, such as sodium lauryl sulfate (i.e. claims 29-30), see column 4, lines 50-54. Absent evidence to the contrary, mercaptoethanol is a synonym for β-mercaptoethanol (i.e.

claims 22 and 23). The use of Na acetate as detailed above teaches all the limitations of claims 24-26. RNAse may be added to facilitate removal of unwanted RNA (column 3, lines 55-58).

Chomczynski teaches a method of DNA purification comprising dissolving cells in a lysing solution (e.g. 4M guanidium thiocyanate, 17% isopropanol, , 0.2% sarkosyl, 0.1M 2-aminoethanethiol HCl, and 0.1M Na acetate, pH 7.0, see Example 1, column 6) followed by addition of 0.15 ml of isopropanol and ethanol to precipitate the DNA (also Example 1, column 7, lines 21-45 and claim 1). Sarkosyl is a detergent, and may be replaced with other sarcosines or polyoxyethylenesorbitan detergents, i.e. claims 29 and 30 (see column 4, lines 53-57). 2-mercaptoethanol may be used in place of 2-aminoethanethiol (column 4, lines 25-29), and absent evidence to the contrary, 2-mercaptoethanol is a synonym for β-mercaptoethanol (i.e. claims 22 and 23). Citric acid may be included in the lysing solution, i.e. as in claim 37 (column 4, lines 53-57). The use of Na acetate as detailed above teaches all the limitations of claims 24-26.

The claimed method of isolating extrachromosomal nucleic acids is essentially disclosed by Little or Padhye with the exception of using an RNAse (Little) or the step recited in claim 3 (Padhye), and the inclusion of a reducing agent, a detergent, a salt as in claim 24, a solvent as in claim 32, or an antioxidant as in claim 37 in the chaotropic solution. The ordinary skilled artisan, seeking a method to purify plasmid DNA, would have been motivated to use an RNAse with the methods of Little because both Padhye and Koller teach this to be a well known reagent having utility for removing unwanted RNA from samples comprising the desired DNA. It would

have been obvious for the skilled artisan to do this because of the known benefit of removing RNA as taught by both Padhye and Koller.

Furthermore, the ordinary skilled artisan, seeking an efficient method to purify plasmid DNA, would have been motivated to use the nucleic acid releasing composition of Koller or the lysing solution of Chomczynski (and the related DNA precipitation steps) in place of the chaotropic solutions and subsequent method steps of Little or Padhye et al. This is because the reagents and methods of both Koller and Chomczynski remove the need to purchase and/or prepare the Celite or glass particles of Little and Padhye et al, respectively. It would have been obvious for the skilled artisan to do this because of the known benefit of isolating extrachromosomal DNA at a lower cost and/or with fewer method steps to save time (and potential loss of the desired DNA). See, for example, column 2, lines 49-63 of Koller.

Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Response to Arguments

Applicant's arguments filed 7/14/2005 have been fully considered but they are not persuasive. As far as the submitted arguments apply to the above rejection, applicants essentially assert that: 1) the claims recite a particular sequence of steps using chaotropic agents without the use of a DNA binding material, limitations not taught by Little et al; 2) the deficiency of Little et al is not remedied by Padhye et al or Fisher et al.

Regarding 1) and 2), in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a particular sequence of steps and absence of a DNA binding material) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Further regarding 1) and 2), all of the claim limitations are taught for reasons set forth above.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Little, Padhye et al, Koller and Chomczynski as applied to claims 1, 3-10, 12-30, and 32-37 above, and further in view of Colpan et al (U.S. 5,747,663, May 5, 1998). **This is a new rejection.**

The teachings of Little, Padhye et al, Koller and Chomczynski are as detailed above and applied as before.

Colpan et al teach the inclusion of Triton X-114 in a chaotropic solution used to prepare plasmid DNA, see e.g. column 1, lines 20-30 and claim 10. The Triton X-114 was included to facilitate removal of unwanted endotoxins from medicaments, for example, plasmid DNA preparations (see columns 1 and 2).

The claimed method of isolating extrachromosomal nucleic acids is essentially disclosed by Little, Padhye et al, Koller and Chomczynski with the exception of using Triton X-114 in the chaotropic solution. The ordinary skilled artisan, seeking a method to prepare plasmid DNA suitable for use as a medicament, would have been motivated to use Triton X-114 in the

chaotropic solutions of Little, Padhye et al, Koller and Chomczynski because Coplan et al teaches Triton X-114 to be a well known reagent of chaotropic solutions having utility for removing unwanted endotoxin from plasmid DNA prepared from bacteria. It would have been obvious for the skilled artisan to do this because of the known benefit of removing endotoxin from plasmids intended as medicaments, as taught by Coplan et al.

Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael D. Burkhart
Examiner
Art Unit 1633